REMARKS

Claims 1-4, 7-9, 13, 19, 20, 31, 32 and 48-52 are pending.

Applicants respectfully request reconsideration in view of the following remarks. Issues raised by the Examiner will be addressed below in the order they appear in the outstanding Office Action.

DETAILED ACTION

Claim Rejections – 35 U.S.C. 112, First Paragraph, Written Description

Claims 1-4, 7-9, 13, 19, 20, 31, 32, 48 and 50-52 are rejected under 35 U.S.C. 112, first paragraph, for allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. Specifically, the Examiner alleges that the specification and claims as originally filed do not provide support for an antibody defined by the CDRs of SEQ ID NOs: 10 and 45 (light chain) and SEQ ID NOs: 18 and 49 (heavy chain).

Applicants respectfully traverse. The CDRs of SEQ ID NOs: 10 and 45 (light chain) and SEQ ID NOs: 18 and 49 (heavy chain) are all from the antibody 1G4 as set forth in Figures 4a and 4b. The light chain is shown as SEQ ID NO:10 in Figure 4a. SEQ ID NO:45 corresponds to the CDR3 of the 1G4 light chain (see paragraph [0094] of the published application, US 2008/0025913) and is identical to amino acid residues 89-97 of SEQ ID NO:10. Therefore claim 1, in defining the light chain using both SEQ ID NO:10 and SEQ ID NO:45, is identical to claiming the 3 light chain CDRs of 1G4 using just SEQ ID NO:10. In particular, claim 1 could alternatively refer to the CDR sequences solely in their context of SEQ ID NO: 10, e.g., residues 24-34 (CDR1), 50-56 (CDR2) and 89-97 (CDR3) of SEQ ID NO:10. The CDR3 region was specifically referred to as SEQ ID NO:45 in claim 1 as opposed to referring to its position in SEQ ID NO:10, e.g., residues 89-97 of SEQ ID NO:10. Similarly, the heavy chain of 1G4 is shown as SEQ ID NO:18 in Figure 4b. SEQ ID NO:49 corresponds to the CDR3 of the 1G4 heavy chain (see paragraph [0094] of the published

application, US 2008/0025913) and is identical to residues 99-105 of SEQ ID NO:18. Therefore, the claims could refer to the heavy chain CDR sequences solely with respect to their position within SEQ ID NO:18, e.g., residues 31-36 (CDR1), 51-66 (CDR2), and 99-105 (CDR3) of SEQ ID NO: 18.

As noted in the previous response, at the time the application was filed, it was well within the purview of the ordinarily skilled artisan to determine the position of the instantly claimed CDRs of a light chain variable region and/or a heavy chain variable region. For example, by comparing the 1G4 variable region amino acid sequences with the variable region amino acid sequences of numerous other murine antibodies, the skilled artisan could have easily and readily determined the "Kabat"-defined CDRs of SEQ ID NOs: 10 and 18. *See*, e.g., Kabat *et al.* (1991) "Sequences of Proteins of Immunological Interest." NIH Publication No. 91-3242, U.S. Department of Health and Human Services, Bethesda, MD.

Furthermore, Applicants assert that the instant specification clearly supports antibodies claimed by reference to their CDR regions. For example, at paragraph [0038] the specification that states,

> "In one embodiment, the antibody includes one or more CDR domains of the antibody. In another embodiment, the antibodies utilized in the present disclosure are humanized antibodies having a light chain variable region comprising at least one CDR selected from the group consisting of amino acid sequences of SEQ ID NO:45 ... In yet another embodiment, the antibodies utilized in the present disclosure are humanized antibodies having a heavy chain variable region comprising at least one CDR selected from the group consisting of amino acid sequences of SEQ ID NO: ... 49 ..." (Emphasis added).

In addition, the specification clearly contemplates humanized antibodies in which the CDRs of mouse monoclonal antibodies disclosed in the specification, such as 1G4, are inserted into a human immunoglobulin framework (see e.g., paragraph [0037] of the published application). As noted above, the claimed antibodies are directed to antibodies comprising the six CDR regions of the 1G4 antibody, e.g., the light chain CDR1, CDR2 and CDR3 from SEQ ID NO:10 and the heavy chain

CDR1, CDR2 and CDR3 from SEQ ID NO:18. Accordingly, one of ordinary skill in the art would have understood that the pending claims are clearly supported by the teachings of the specification.

Finally, Applicants wish to point out to the Examiner that Figure 4b contains an alignment of various heavy chain sequences, including SEQ ID NO:18. The alignment introduced gaps where appropriate in order to line up the corresponding residue in each sequence. As a result, SEQ ID NO:18 as depicted in Figure 4b has gaps at positions 56, 105 and 106 of the guiding numbering scheme at the top of the alignment. Therefore, the residues of SEQ ID NO:18 as labeled in Figure 4b are different from the actual amino acid residue positions within SEQ ID NO:18 as listed in the Sequence Listing. The claims refer to the appropriate amino acid residues within the context of SEQ ID NO:18 in the Sequence Listing.

In view of the above, Applicants submit that one of skill in the art would have understood that the application clearly supports the pending claims and that applicants were in possession of the claimed invention. Withdrawal of the rejection is respectfully requested.

CONCLUSION

In view of the above amendments, Applicants believe the pending application is in condition for allowance. The Examiner is invited to telephone the undersigned to discuss any issue pertaining to this response. Applicants request favorable consideration of the application and early allowance of the pending claims.

Applicants believe no fee is due with this response. However, if a fee is due, please charge our Deposit Account No. 18-1945, under Order No. ALEX-P01-112 from which the undersigned is authorized to draw.

Dated: April 22, 2010

Respectfully submitted,

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